**Comparison of two commercial dentifrices in the reduction of gingivitis and plaque: a randomized clinical trial**

**Abstract**

**Objectives:** Chlorhexidine (CHX) and triclosan are the most used chemical agents in dentistry. However, the combination of these products has never been tested. We hypothesize that the addition of CHX to a triclosan dentifrice formulation may offer additional benefits in the reduction of plaque and gingivitis. Thus, the aim of this study was to compare a commercial dentifrice containing 0.05% chlorhexidine and 0.3% triclosan, with conventional toothpaste containing 0.3% triclosan, in the treatment of gingivitis and plaque reduction.

**Materials and methods:** Thirty volunteers were randomly assigned to receive a dentifrice containing 0.05% CHX and 0.3% triclosan or a dentifrice containing basically 0.3% triclosan. Subjects received clinical evaluation such as gingival index (GI) and plaque index (PI) at baseline, 30 and 60 days.

**Results:** After 60 days, both treatments led to a significant improvement in GI and PI. There was no significant difference between groups as regards change in GI and PI (p>0.05).

**Conclusion:** The combination of 0.05% CHX with 0.3% triclosan did not offer further benefits to gingival inflammation and plaque control when compared with a dentifrice containing 0.3% triclosan.

**Key words:** chlorhexidine; CHX dentifrice; triclosan; plaque; gingivitis.

**Comparação de dois dentífricos comerciais na redução da gengivite e da placa bacteriana: um ensaio clínico randomizado controlado**

**Resumo**

**Objetivos:** Clorexidina e triclosan são os agentes químicos mais utilizados em odontologia. No entanto, a combinação desses produtos nunca foi testada. Nós levantamos a hipótese de que a adição de clorexidina a um dentifrício contendo triclosan pode oferecer benefícios adicionais na redução de placa e gengivite. Assim, o objetivo deste estudo foi comparar um dentífrico comercial contendo 0,05% de clorhexidina e 0,3% de triclosan, com creme dental convencional contendo 0,3% de triclosan, no tratamento de gengivite e redução da placa.

**Materiais e métodos:** trinta voluntários foram distribuídos aleatoriamente para receber um dentifrício contendo 0,05% de clorexidina e 0,3% de triclosan ou um dentifrício contendo basicamente 0,3% de triclosan. Os indivíduos receberam avaliação clínica de índice gengival (IG) e índice de placa (IP) na tem 0, 30 e 60 dias.

**Resultados:** após 60 dias, ambos os tratamentos levaram a uma melhora significativa no IG e IP. Não houve diferença significativa entre os grupos no que se refere à mudança na GI e PI (p> 0,05).

**Conclusão:** A combinação de 0,05% de Clorexidina com 0,3% de triclosan não ofereceu benefícios adicionais para a redução de inflamação gengival e o controle da placa quando comparado com um dentifrício contendo 0,3% de triclosan.

**Palavras-chave:** Clorexidina; Triclosan; Índice de placa; Índice gengival.

**Introduction**

Gingivitis is characterized by a reversible periodontal inflammation associated with biofilm[1]. Epidemiological studies have shown a high prevalence of this condition, involving over half of the US population [2]. Daily mechanical control by tooth brushing and dental flossing has been shown to be effective in the treatment and prevention of gingivitis. However, achieving an adequate plaque control is difficult for most people[3]. Mechanical control alone reduces dental plaque to 30-50% only[4]. The result is a high prevalence of dental plaque, dental calculus and gingival bleeding, as shown in epidemiological studies[5]. In this context, the development of new and diverse dentifrice compositions is important in order to optimize the effectiveness of plaque control. Several agents have been studied for their plaque-inhibitory action such as triclosan, sodium fluorideand chlorhexidine[3, 4, 6,7].

Chlorhexidine (CHX) is an antiseptic with a broad antimicrobial action, including a wide range of Gram-positive and Gram-negative bacteria. Its dental plaque inhibition properties were first investigated by Schroeder[8], and it was confirmed as later by as an effective agent in preventing gingival inflammation and reduction of plaque by Löe and Schiott[9]. Since then, it has played a central role in research, being used in many vehicles such as gels, varnishes, chips, chewing gums, dentifrices and mouthwashes[10-12]. In dental practice, mouthwash is the most used form, though clinical studies has shown that CHX in dentifrices can also offer further benefits to oral health with less tooth discoloration[13]. Moreover, a meta-analysis performed in 2014 showed that CHX dentifrices provide a significant benefit on the treatment of gingivitis and plaque inhibition[14]. Besides that, when used for long periods, CHX has shown to produce local side effects such as tooth stainingand taste disturbance[15,16].

Like chlorhexidine, triclosan (2’-hydroxy-2,4,4’-trichlorodiphenyl ether) is also a wide-spectrum antimicrobial agent[17]. Due to lower incidence of adverse effects, it has been preferably used as an adjunct to mechanical oral hygiene. Triclosan can significantly reduce gingival inflammation and plaque accumulation[6,18,19]. Some studies showed anti-inflammatory properties, reducing interleukin (IL) 1β, IL-6, tumor-necrosis factor, and prostaglandins (PG)[3,20]. In addition, when used as adjunct to tooth brushing, triclosan also reduce microorganisms related to periodontal disease such as *Fusobacteria sp* and *Veillonella sp*[21,22]. The literature shows that the use of triclosan as an adjunct to toothbrush provides clinical benefits in comparison with placebo[6,23,24].

The addition of CHX to a triclosan dentifrice formulation may offer additional benefits in the reduction of plaque and gingivitis. However, so far, no study has compared the combination of these two substances with a triclosan dentifrice.

Thus, the aim of this randomized clinical trial was to compare a commercial dentifrice containing chlorhexidine plus triclosan with a conventional toothpaste containing triclosan, in the treatment of gingivitis and plaque reduction.

**Materials and methods**

***Trial Design and participants***

This was a randomized, double-blind, two-arm parallel-group controlled trial. Participants were selected among those seeking dental treatment at UNESP – São Paulo State University (São José dos Campos, Brazil). The inclusion criteria were: 1. good general and oral health, 2. at least twenty-four teeth in mouth, 3. 18-35 years old. Exclusion criteria were: 1. smoking, 2. Presence of braces or other orthodontic appliances, 3. use of antibiotics 6 months prior to the study.

All subjects received intraoral examination and answered a questionnaire comprising questions regarding medical and dental history. The subjects who fulfilled the inclusion criteria were invited to participate in the study. All individuals who agreed to participate were informed about the nature, potential risks and benefits of the study and signed a term of free informed consent. The study was approved by the Ethics Committee of UNESP- Institute of Science and Technology, under the protocol 41294914.7.0000.0077.

***Interventions and procedures***

One of the investigators (W.D.K.) was responsible for participant’s enrollment and assignment to interventions. The study coordinator (E.S.R) used a computer-generated sequence to randomly assign the subjects to the following two groups: i) Test (chlorhexidine and Triclosan): Dentifrice produced by Pharmakin, containing chlorhexidine digluconate 0,05%, triclosan 0.30 % and zinc lactate 0.50 %, and ii) Control (sodium Fluoride 1450 ppm, Triclosan 0,3% and copolymer (Colgate Total 12®, Colgate Palmolive Co.). Both dentifrices (test and control) were packaged into identical tubes containing the number to which the participants were assigned.

Initially, all subjects received prophylaxis oral hygiene instructions. The subjects were instructed to use the same toothbrush, dental floss (Kinextra soft, Espanha) and not to use any oral antiseptic solution during the study period. Moreover, the subjects were instructed to use the same amount of the assigned dentifrice during the toothbrushing, which was performed during two minutes, three times a day, during the study period.

***Outcomes and blinding***

The primary outcome variable was mean GI reduction (baseline - 60 days). Secondary outcome variables were mean PI and tooth staining after 60 days and PI reduction (baseline – 60 days).

The following clinical parameters were evaluated at baseline, 30 and 60 days: Gingival index (GI)[25], Plaque index (PI)[26] and Tooth staining (absent/present). Further, the subjects were asked about any adverse effect of the toothpaste during the study.

A single examiner (HVB) performed all clinical examinations. The examiner did not know which dentifrice each participant received. Participants and personnel providing treatment were not aware about the content of their assigned dentifrice.

***Statistical analyses***

Mean clinical parameters were computed for each subject and then for each group. Intragroup and intergroup mean differences in GI and PI were evaluated by ANOVA. Student’s T-test was used to compare intergroup mean difference as regards age. Fisher´s exact test was used to evaluate association between group and tooth staining or gender.

**Results**

***Subject retention, compliance and adverse effects***

Thirty subjects were selected for the study. All participants remained until the end of the follow-up period. Flow chart of the study design is presented in Figure 1. Table 1 depicts clinical and demographic information of the patients. No significant differences were found between the two groups as regards age, gender and baseline clinical parameters (p>0.05). All subjects reported having followed the instructions during the 60 days of the study.

Two individuals from the Test Group presented tooth discoloration. The other subjects did not report any side effects associated with the substances used.

Table 1. Demographic characteristics and mean ± SD clinical parameters at baseline, 30 and 60 days.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   |   |   |   | **Treatment groups** |   |   |
| **Variable** | **Time point** | **Test** | **Control** | **One-way ANOVA** |
|   |   |   |   | n=15 | n=15 | p-value |
| Gender | Baseline |  3/12 | 2/13 | 1.000 |
|  (Male/Female) |  |  |  |  |  |  |  |  |  |  |
| Age(Years) | Baseline | 26.27 ± 1.24 | 25.07 ± 0.85 | 0.4340 |
| GI | Baseline | 0.37 ± 0,24 | 0,49 ± 0,24 | p>0,05 |  |
|  | 30 days | 0.28 ± 0,14 | 0,39 ± 0,29 | p>0,05 |  |
|  |  | 60 days | 0,12 ± 0,08\* | 0,26 ± 0,19\* | p>0,05 |  |
| PI | Baseline | 0.76 ± 0,52 | 0.76 ± 0,45 | p>0,05 |  |
|  |  | 30 days | 0,45 ± 0,34 | 0,48 ± 0,31 | p>0,05 |  |
|  |  | 60 days | 0.35 ± 0,34\* | 0.33 ± 0,24\* | p>0,05 |  |
| Tooth staining | Baseline | 0/15 |  | 0/15 |  | p>0,05 |  |
| (presence/ absence) |  | 30 days | 2/13 |  | 0/15 |  | p>0,05 |  |
|  | 60 days | 2/13 |  | 0/15 |  | p>0,05 |  |

The significance of differences between baseline, 30 and 60 days was assessed using repeated measures ANOVA and Student t-test. Fisher’s T-test was used for categorical variables.

The significance of differences between baseline, 30 and 60 days was \* Indicate significant differences between time points.

Test group: Dentifrice containing chlorhexidine digluconate 0,05%, triclosan 0.30 % and zinc lactate 0.50 %; Control group: Dentifrice containing basically sodium Fluoride (1450 ppm) and Triclosan 0,3%. GI: gingival index; PI: plaque index

***Clinical outcomes***

No statistically significant differences were observed between groups for age, gender, GI, PI and tooth discoloration at baseline, 30 and 60 days (p > 0.05). After 60 days, both treatments led to a significant improvement in GI and PI.

Table 2 shows the changes in mean GI and PI between baseline and 60 days. There was no difference between groups as regards change in GI and PI.

**Table 2.** Mean and SD GI and PI reduction between baseline and 60days.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
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|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   |   |   |   | **Treatment groups** |   |   |
| **Variable** | **Time point** | **Test** | **Control** | **Student t-test** |
|   |   |   |   | n=15 | n=15 | p-value |
| GI | 0-60 days | 0.25 ± 0,23 | 0.22 ± 0,27 | p>0,05 |
| PI | 0-60 days | 0.41 ± 0.10 | 0.43 ± 0.08 | p>0,05 |

Test group: Dentifrice containing chlorhexidine digluconate 0,05%, triclosan 0.30 % and zinc lactate 0.50 %; Control group: Dentifrice containing basically sodium Fluoride (1450 ppm) and Triclosan 0,3%. GI: gingival index; PI: plaque index

**Discussion**

The results of this randomized clinical trial showed that both dentifrices led to a significant improvement in clinical parameters, although no significant difference between the two groups were found. After 60 days, the clinical improvements observed in both groups were more compatible with studies that investigated the effect of a daily toothbrushing with a triclosan dentifrice[23,28,29] than studies with CHX [30-32]. In this study, the incorporation of 0.05% chlorhexidine in a dentifrice containing 0.3% triclosan (Test Group) did not offer further benefits to gingival inflammation and plaque control in comparison with a dentifrice containing 0.3% triclosan (Control Group).

The GI reduction of 0.25 and 0.22 observed in the Test and Control groups, respectively, are in agreement with other trials which assessed the effects of a dentifrice containing triclosan in these clinical parameters[27-29]. Moreover, in a meta-analysis performed by Hioe & van der Weijden[23], the authors found an IG reduction of 0.24 and 0.48 in PI, favoring triclosan. The results of this meta-analysis are similar to those of the present study.

CHX is the most effective anti-plaque and anti-gingivitis chemical agent in dentistry[14]. When associated to dentifrices, it has been successfully tested and used in order to enhance mechanical plaque control[14]. However, in this present trial, the association of 0.05% CHX with 0.3% triclosan did not result in additional benefits to gingival inflammation and plaque control in comparison with a dentifrice containing 0.3% triclosan.

An important issue to be considered is the low-dose 0.05% CHX used in the Test Group. The dose-dependent anti-plaque effects of CHX have been shown *in vivo* studies[33,34]. Hoffmann[35] assessed the clinical effects of rinsing with a low-dose 0.06% CHX in comparison with a commercially available 0.1% CHX. At the end of the trial, the authors suggested a minimum concentration of 0.1% CHX if a further decrease in GI is desired.

Furthermore, there are no comparative studies regarding the triclosan when associated with other substances such as CHX, in gingival parameters. Thus, there is no evidence that this association might enhance the anti-gingivitis and anti-plaque effect. Mendes[36] assessed the effects of rinsing 0.05% chlorhexidine, 0.15% triclosan and 0.18% zinc pidolate on bad breath. At the end of the study, the authors demonstrated a significant effect on this outcome, however, no major comparisons can be made since the vehicle and outcome assessed were different from the present study.

When CHX is used for long periods, tooth discoloration is the side effect most expected. At 60 days, only two individuals from the Test Group presented tooth staining. This fact might be explained by the low-dose 0.05% CHX used in the Test group. Moreover, there is evidence that the dose-dependent anti-plaque effect can be applicable in regards to tooth discoloration[14,37]. Therefore, a slight tooth staining was expected in this study.

Since this trial has limitations, the results of the present study might be interpreted with caution. The short-term follow-up period of 60 days and the small sample size (n=15) might have interfered in the results. Thus, the results presented here suggests that the combination of 0.05% CHX with 0.3% triclosan did not offer further benefits to gingivitis reduction and plaque control when compared with a dentifrice containing 0.3% triclosan. Nevertheless, more studies are needed to corroborate these findings.

**Conclusion**

The combination of 0.05% CHX with 0.3% triclosan did not offer further benefits to gingival inflammation and plaque control when compared with a dentifrice containing 0.3% triclosan.

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